REMARKS

Claims 1-29 are pending in this application. Claims 1, 2, and 8 are amended herein, and new claims 14-29 are added. Support for the amendments and new claims can be found throughout the specification and claims as filed, e.g., at page 4, lines 18-27; page 5, lines 4-6; page 6, lines 5-10; page 6, line 16 bridging to page 7, line 2; page 7, lines 26-29; and page 25, lines 7-13. New claim 16 is supported by the subject matter of original claim 1(d). No new matter has been added. All of the amended and new claims are properly included in the elected group, Group I.

Sequence Listing

The specification was objected to for allegedly not complying with the sequence rules of 37 CFR §§ 1.821-1.825 for not including sequence identifiers for the sequences disclosed in Figures 1 and 2. As the Examiner helpfully suggested, applicants have amended the Brief Description of the Drawings to incorporate sequence identifiers corresponding to sequences present in the sequence listing as originally filed. No new matter has been added by this amendment. Applicants submit that the application complies fully with the sequence rules.

Title

The title was objected to as allegedly not descriptive. Applicants have amended the title to read, "Genes Encoding Mast Cell-Derived Membrane Proteins."

Claim Objections

Claims 1, 2, 4-6, and 8 were objected to for reading on non-elected embodiments in the recitation of SEQ ID NOs: 3 and 4. Applicants have amended claims 1 and 8 to delete the non-elected subject matter. Applicants request withdrawal of the rejection.

35 USC § 101

Claims 1, 2, 4, 5, and 8 were rejected as allegedly directed to non-statutory subject matter. The Office Action states that the claims read on naturally occurring nucleic acids. Applicants have amended claims 1 and 8 to recite that the nucleic acids are "isolated." Accordingly, applicants request reconsideration and withdrawal of the rejection.

35 USC § 112, first paragraph

Claims 1, 2, 4-6, and 8 were rejected as allegedly failing to comply with the written description requirement. To satisfy the written description requirement, a patent specification must describe the invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. The U.S. Patent and Trademark Office's Written Description Training Materials (Revision 1, March 25, 2008) are helpful in determining whether the written description requirement is satisfied.

Claim 1 encompasses a genus of nucleic acids that encode the polypeptide of SEQ ID NO:2, as well as those that encode any polypeptide having an amino acid sequence in which up to 30 amino acids in the amino acid sequence of SEQ ID NO:2 have been replaced, deleted, inserted, and/or added.[1] As with claim 1 of Example 11B of the Written Description Training Materials, based on the disclosure of SEQ ID NO:2, one skilled in the art could list all of the nucleic acid sequences that encode a polypeptide in which up to 30 amino acids of SEQ ID NO:2 have been replaced, deleted, inserted, and/or added (see page 41). The level of skill and knowledge in the art is such that one of ordinary skill using the guidance in the specification would be able to use conventional sequencing and nucleic acid synthesis to routinely generate such nucleic acids. Therefore, one of ordinary skill in the art would conclude that the applicant was in possession of the claimed genus at the time of filing.

New claim 16 (derived from original claim 1(d)) encompasses a genus of nucleic acids that specifically hybridize with the entirety of a probe consisting of the complement of SEQ ID NO:1 under highly stringent conditions. This is similar to claim 3 of Example 6 of the Written

[1] As SEQ ID NO:2 includes 318 amino acids, replacement of 30 amino acids within the sequence yields a polypeptide ~90.6% identical to SEQ ID NO:2.

Description Training Materials, except that claim 16 does not recite a function of polypeptides encoded by the claimed nucleic acids (see page 21). As stated in the Written Description Training Materials at page 22 in describing the hypothetical Example 6:

> Because hybridization under highly stringent conditions requires a high degree of structural complementarity, nucleic acids that hybridize to the complement of SEQ ID NO:1 will likely share many nucleotides in common with SEQ ID NO:1. Thus, the claimed genus necessarily includes partial structures of SEQ ID NO:1. The disclosure of SEQ ID NO:1 combined with the knowledge in the art regarding hybridization would put one in possession of the genus of nucleic acids that would hybridize under stringent conditions to SEQ ID NO:1.

Since exactly the same reasoning applies to the present facts, one of ordinary skill in the art would conclude that applicants were in possession of the genus of DNAs encompassed by claim 16 at the time of filing of the application.

Claim 8 encompasses a genus of polynucleotides that include a segment of SEQ ID NO:1 or the complementary strand thereof, wherein the segment of SEQ ID NO:1 is at least 15 nucleotides in length. This is similar to claim 1 of Example 4B of the Written Description Training Materials, which recites an isolated nucleic acid comprising a portion of a protein-encoding open reading frame (page 13). The genus of nucleic acids encompassed by claim 8 correspond to nucleic acids that include portions of the cDNA described by SEQ ID NO:1 its complement. There may be substantial variability among the species of nucleic acids encompassed by the claim because the at least 15 nucleotides that are complementary to SEQ ID NO:1 or its complement may be combined with other DNA sequences. However, the scope of the genus is defined by the presence of the partial structure of SEQ ID NO:1. All members of the genus will predictably include at least 15 nucleotides of SEQ ID NO:1 or its complement. One skilled in the art could list all of the partial sequences of SEQ ID NO:1 or its complement that include at least 15 nucleotides of SEQ ID NO:1 or its complement and would be able to use conventional sequencing and nucleic acid synthesis to routinely generate such nucleic acids. Therefore, one of ordinary skill in the art would conclude that the applicant was in possession of the claimed genus at the time of filing.

Claims 2, 28, and 29 specify nucleic acids that encode variants of SEQ ID NO:2 that bind to a SHP-1 protein, a SHP-2 protein, or a SHIP protein. Such variants have up to 30 amino acids in the amino acid sequence of SEQ ID NO:2 replaced, deleted, inserted, and/or added; up to ten amino acids in the amino acid sequence of SEQ ID NO:2 have been replaced, deleted, inserted, and/or added; or are 85% or more identical to SEQ ID NO:2. These claims are similar to the claims discussed in Example 11B of the Written Description Training Materials. The specification discloses that a chimeric polypeptide containing the intracellular portion of SEQ ID NO:2 binds to the intracellular proteins SHP-1, SHP-2, and SHIP (see Example 5) and identifies four conserved motifs of SEQ ID NO:2 believed to be important for the binding activity (see Fig. 1). These sequences are predicted to be immunoreceptor tyrosine-based inhibitory motifs (ITIMs), which are short, loosely conserved motifs found in the intracellular domains of various signaling proteins (page 161, col.1 of Billadeau and Leibson, J. Clin. Invest., 109:161-168, 2002, already of record). Phosphorylation of the tyrosine of an ITIM motif allows for binding to SH2 domain-containing proteins, including SHP-1, SHP-2, and SHIP (page 165 of Billadeau and Leibson). The specification also demonstrates that tyrosine phosphorylation of the chimeric polypeptide containing the intracellular portion of SEQ ID NO:2 is required for binding to SHP-1, SHP-2, and SHIP-1, further supporting the prediction that SEQ ID NO:2 includes functional ITIM motifs. Because the specification identifies conserved domains responsible for binding to SHP-1, SHP-2, and SHIP-1, one of ordinary skill in the art with knowledge of the consensus ITIM motifs would be able to predict substitutions within these sequences that would retain SHP-1, SHP-2, and SHIP-1 binding activity. Further, one of ordinary skill in the art would predict that amino acid substitutions outside of the identified domains would be unlikely to greatly affect binding activity. Thus, a correlation exists between the binding activity of the claimed polypeptide-encoding nucleic acids and the disclosed structural domains. The art-recognized correlation between the structure of ITIM motifs and their binding activity is sufficient to overcome the unpredictability allegedly taught by Attwood and Skolnick (Office Action, page 10). Based on the applicants' disclosure and the knowledge within the art, those of

ordinary skill in the art would conclude that the applicant was in possession of the claimed genera at the time of filing.

Based on at least the above, applicants submit that all claims are in compliance with the written description requirement of section 112, paragraph 1, and request reconsideration and withdrawal of the rejections.

Claims 1, 2, 4-6, and 8 were rejected as allegedly not enabled. The Office Action states that undue experimentation would be required to make and use the invention as claimed. Applicants traverse.

The level of skill and knowledge in the art and the guidance in the specification is such that one of ordinary skill would be able to use conventional sequencing, nucleic acid synthesis, and hybridization to routinely generate the claimed nucleic acids, including nucleic acids that encode polypeptides of SEQ ID NO:2 and the claimed variants thereof. Further, the specification teaches in detail how to make such variants and test the variants to see whether they bind to SHP-1, SHP-2, and SHIP. Further, the specification describes art-recognized ITIM motifs that are demonstrated to be important for the binding activity (see above). Even if molecular biology is assumed to have been unpredictable at the time of filing, the level of skill in the relevant art of making and testing variant nucleic acids and polypeptides was high. Based on the guidance in the specification, the prior art teachings regarding ITIM motifs, and the level of one of skill in the art, undue experimentation would not have been required to make and use the claimed nucleic acids. Applicants request reconsideration and withdrawal of the rejection for alleged lack of enablement.

The Office Action also asserts a second ground for rejection of claims 1 and 2 for lack of enablement. The Office Action asserts, at page 8, that SEQ ID NO:2 is capable of binding to SHP-1, SHP-2, and SHIP, but not DAP10, DAP12, or FcRγ. Without conceding the merits of this rejection, applicants have amended claim 2 to delete references to DAP10, DAP12, or FcRγ. This moots the rejection.

35 USC § 102

Claims 1, 2, 4, 5, and 8 were rejected under 35 USC § 102(b) as allegedly anticipated by GenBank Accession Number AK045869 (alleged publication date of 1999). Applicants point out that this reference is not available as prior art against the claims because its actual publication date falls after the priority date of the application. Applicants investigated the detailed revision history of this GenBank entry, submitted herewith as Exhibit A (downloaded from the NCBI website on June 5, 2008). Although this reference cites a document published in 1999, the actual publication date of the record cited by the Examiner is apparently September 7, 2005.[2] The revision history clearly states that "Accession AK045869 was first seen at NCBI on Dec 10 2002 1:28 PM." Applicants also enclose herewith as Exhibit B a copy of Accession Number AK045869 as first seen on that date.[3]

Further, none of the publications cited by Accession Number AK045869 that fall before the earliest priority date of this application (Carninci and Hayashizaki, Meth. Enzymol. 303:19-44, 1999; Carninci et al., Genome Res. 10:1617-30, 2000; Shibata et al., Genome Res. 10:1757-71, 2000; and Kawai et al., Nature 409:685-690, 2001, submitted herewith as Exhibits C-F, respectively) teaches or suggests the sequence described in Accession Number AK045869.

Applicants submit herewith certified translations of the priority documents Japanese Application No. 2002-316680, filed on October 30, 2002, and Japanese Application No. 2002-354165, filed on December 5, 2002, thus perfecting the priority claim. Because the earliest publication date of Accession Number AK045869 (December 10, 2002) falls after the priority date(s) of this application, Accession Number AK045869 is not available as prior art against this application. Applicants request withdrawal of the rejection for alleged anticipation.

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[2] The September 5, 2002, date listed on the third line of the reference cited by the Examiner is the modification date of the entry, which was presumably updated on September 7, 2005, as indicated on the Revision History.

[3] As in the above footnote, the December 5, 2002, date listed on Exhibit B is presumably the creation date of the entry, which was published December 10, 2002, as indicated on the Revision History.

35 USC § 103

Claims 1, 5, and 6 were rejected as allegedly obvious over GenBank Accession Number AK045869. As described above, this reference is not available as prior art against the instant claims. Therefore, applicants request withdrawal of the rejection for alleged obviousness.

Concluding Remarks

In light of the arguments made herein, applicants submit that the pending claims are patentable and request early and favorable action thereon. If the Examiner feels it would further prosecution of the present case, he is invited to telephone the undersigned at 617-521-7020.

Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

This reply is being submitted along with a Petition for Extension of Time and the required fee. Please apply any other charges or credits to Deposit Account 06-1050, referencing Attorney Docket No. 14875-142US1.

Respectfully submitted,

Date: June 6, 2008

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